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A Positive Pregnancy Test in the Post-Menopausal Psychiatric Patient—*What to Think?*

ABSTRACT

Assaying the serum β-hCG is the pregnancy test employed to verify an early pregnancy. It becomes positive at approximately 10 days after conception. Knowing whether or not a patient is pregnant is critical to avoid exposure to medications or procedures that might be teratogenic. Psychiatric patients are sometimes suboptimal historians, so such β-hCG testing is especially worthwhile to assure recognition of an active, early-stage pregnancy.

In normal pregnancy, the serum β-hCG level doubles every 2 to 3 days for the first eight weeks or so. Minimally raised, non-escalating β-hCG concentrations are documented in non-pregnant, post-menopausal women. Repeating the assay in 12 to 36 hours would help to clarify a non-pregnant status, because there is no rapid escalation in the post-menopausal β-hCG level. In normal pregnancy, expect at least a 30-percent increase in β-hCG concentration over this time period. Ectopic pregnancies, some neoplasia, and other conditions may also elevate the β-hCG, but again, not in the escalating patterns of normal pregnancy. In those cases, further workup may be needed. The very rapid, accurate detection of an early pregnancy is an important part of safe medical practice and better patient care.

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INTRODUCTION

The principle of doing no harm is important in medical care. Safe practice includes identifying pregnant patients. Many physicians routinely utilize serum beta-human chorionic gonadotropin (β-hCG) testing as a screening aid to detect early pregnancy; this allows discretion in ordering radiological procedures and judicious use of pharmaceuticals to avoid potential teratogenic effects. On our psychiatry in-patient service, we order a pregnancy screening test on all potentially pregnant women. We recommend this even in women of an age when menopause is likely but not confirmed. The small additional expense of testing is justified by the added safety.

The serum β-hCG becomes positive in a pregnancy at approximately 10 days after fertilization. The level then escalates dramatically. Occasionally, one may discover a positive serum pregnancy screening test with a slightly elevated β-hCG assay in non-pregnant women. Such a laboratory finding in a woman suspected to be menopausal can yield uncertainty about her pregnancy status.

The following vignettes illustrate two examples of such a quandary. The discussion aims to clarify understanding the β-hCG values in post-menopausal women. Rapid identification of pregnancy or ruling it out is important clinically to aid the selection of appropriate diagnostic studies and/or to help in treatment decisions.

Case 1. A 53-year-old Caucasian woman was hospitalized in a manic state with a history of bipolar disorder and hypothyroidism. Lithium and risperidone were her most recent medications. The patient said she was pregnant. She reported weight gain and breast engorgement and claimed that she could feel fetal movements. Physical examination evidenced obesity and bilateral lower leg edema, but no enlargement of the uterus.

Admission laboratory workup was remarkable only for a thyroid stimulating hormone (TSH) level of 17.5mIU/mL and a positive serum β-hCG pregnancy screening test. A quantitative assay documented a β-hCG level at 6.2mIU/mL. Further quantitative β-hCG results over several subsequent days revealed concentrations of 6.2, 5.7, and 7.0mIU/mL.

This pattern of weakly positive β-hCG levels is compatible with postmenopausal findings and may be partly related to interference by the elevated TSH. The assays did not show an escalating pattern. The patient was considered not to be pregnant. Psychiatric and endocrine treatments were initiated in a conventional regimen.

Case 2. A 59-year-old Caucasian woman was hospitalized in a psychotic state. She had a history of hypertension and was not taking any medications. In the remote past, substance abuse had been present. Clinically, the patient exhibited bizarre behavior and hallucinations. Physical examination was within normal limits.

Admission laboratory assessment included a negative toxicology screen of blood and urine and a positive serum β-hCG pregnancy test. Quantification revealed results at 13.6mIU/mL. Serum β-hCG concentrations over the next three days were reported as 15.3, 18.2, and 16.9mIU/mL, respectively.

Pregnancy was ruled out, with clinical findings favoring a postmenopausal hormone pattern. Psychopharmaceutical management was then prescribed in a routine manner.

DISSUSSION

Human chorionic gonadotropin is a glycoprotein hormone primarily secreted in significant amounts by the placenta during pregnancy. It consists of two subunits, alpha and beta; the alpha component is identical to that of TSH, luteinizing hormone (LH), and follicle stimulating hormone (FSH).[1] A pregnancy test is interpreted as positive when β-hCG levels are 5mIU/mL or greater. Normal pregnancy results in exponentially increased secretion of β-hCG, roughly doubling every 2 to 3 days until approximately eight weeks of gestation.[2] Then the concentration gradually declines. Low concentrations of β-hCG are seen in healthy male patients and non-pregnant female patients, with the pituitary gland as the primary source. Slightly raised β-hCG levels are also seen in some normal post-menopausal women. The β-hCG concentration in these older, non-pregnant women may routinely be as high as 8mIU/mL and even slightly more in some individuals. Other potential causes of elevations include ectopic pregnancy,[3] liver or gastrointestinal disorders,[4–6] trophoblastic or germ cell tumors,[7,8] and certain non-trophoblastic neoplasia.[9,10]

Ectopic pregnancy is an implantation of a fertilized ovum outside the uterine cavity;[8] in 90 percent of the cases, the fallopian tube is the primary site. Ectopics result in increasing β-hCG concentrations.[11] However, if the β-hCG escalates less than 66 percent in 48 hours during the first eight weeks of gestation, then an ectopic pregnancy is strongly considered.[3]

Elevated and rising β-hCG levels are documented in a variety of neoplastic conditions, including trophoblastic pathologies, germ cell tumors, and certain other cancers.[7] Gestational trophoblastic diseases are uncommon but curable tumors arising from the product of conception. The two major categories of gestational trophoblastic neoplasia are hydatidiform mole and choriocarcinoma. Hydatidiform mole is usually benign or locally invasive, while choriocarcinoma may metastasize. The β-hCG values are high in these patients, and levels can rapidly escalate as a disease and follow-up marker.[8] Malignancies of

lung, liver, breast, bladder, and gastrointestinal tract are also sometimes associated with secretion of β-hCG.[9,10]

Since newly hospitalized psychiatric patients are often compromised historians, screening the women for pregnancy is important. It remains a physician's individualized clinical judgment to determine at what age pregnancy testing is no longer required. It is critical for the psychiatrist to know his or her patient's pregnancy status because many pharmaceuticals, like lithium or divalproex, are potentially teratogenic. When a serum pregnancy test is reported as positive, quantifying the β-hCG level is a reasonable next step. Normal pregnancy initially results in rapid doubling of β-hCG concentrations, every 2 to 3 days. Failure to elevate in this way excludes normal pregnancy, but an ectopic or non-pregnant condition then becomes a consideration. Serially following the quantitative β-hCG will help settle this diagnostic dilemma. Non-pregnant, non-neoplastic cases of β-hCG elevation can result from hepatic cirrhosis, duodenal ulcer, and inflammatory bowel disease.[4-6] More work up may be required.

Post-menopausal women sometimes exhibit elevations in β-hCG that may cause the serum pregnancy test to be reported as positive; however, such patients are not pregnant. As noted, some normal, non-pregnant, post-menopausal women do have β-hCG levels that are slightly above normal laboratory limits (5–8mIU/mL) and without an increasing pattern over time. Further elevations after menopause might suggest the presence of hepatic disease[5,6] or a tumor (e.g., of the lung)[9] and often trigger more investigation. Although the patient in Case 2 had β-hCG levels as high as 18.2mIU/mL, the non-escalating pattern and clinical picture were considered more suggestive of normal menopause than of some other etiology.

In summary, some non-pregnant, post-menopausal women have mildly elevated β-hCG levels without escalations in serially assessed concentrations. Other conditions may also raise levels, though not showing the rapid doubling characteristic as seen in normal pregnancies.

Whenever an older woman has a positive pregnancy test, the physician should follow up with serial β-hCG testing. Doubling of the β-hCG assay in normal pregnancy is experienced every 2 to 3 days; however, increases in β-hCG concentrations are progressively recognized over even shorter time intervals. A significant upsurge in 24 to 36 hours, for instance, is suggestive of pregnancy. In our clinical experience, a 30-percent rise in the level is significant for a pregnancy; this degree of elevation may be detectable in as little as 12 hours. A slightly raised, non-escalating level of β-hCG, without any evidence of other pathology, is consistent with menopause. Moderately elevated concentrations generally prompt more evaluation and follow-up. Ultimately, the clinical severity of the case dictates treatment decisions, but a rapid determination of pregnancy status is vital to improving outcomes.

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